REMARKS

Claim Rejections – 35 USC §112

Claims 1 to 16 have been rejected as containing subject matter which has not been described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is argued in the Office Action that "[a] review of the disclosure fail to find the nucleotide sequence for any and all gyrB genes as found in any and all microorganisms. In order to practice the invention, one would first need to sequence the gyrB gene in any and all microorganisms and to have that resource at the ready in order to conduct the requisite comparison step. ... Such non-disclosure on the part of applicant unfairly shifts the burden of enablement from applicant to that of the public."

Applicants respectfully submit that the invention as claimed in claims 1 to 16 is enabled by the specification for the following reasons. Arguments below is made with respect to claim 1 but the same arguments equally apply to all other independent claims with similar claim recitations as claim 1.

Claim 1 as amended recites:

> 1. (Currently Amended) A method for identifying a microorganism, comprising:
> (1) synthesizing forward and reverse primers based on a single pair of amino acid sequences selected from the group consisting of the SEQ ID NOS: 69 and 74, SEQ ID NOS: 69 and 78, SEQ IDS NOS: 72 and 71, SEQ ID NOS: 72 and 74, SEQ ID NOS: 72 and 78, SEQ ID NOS: 69 and 70, SEQ ID NOS: 71 and 74, SEQ ID NOS: 72 and 75, SEQ ID NOS: 69 and 76, and SEQ ID NOS: 78 and 79;
> (2) amplifying *gyrB* gene DNA from the microorganism using said two primers to produce a *gyrB* gene DNA fragment;
> (3) isolating said DNA fragment;
> (4) determining the nucleotide sequence of said DNA fragment; and
> (5) **comparing the sequence of the amplified *gyrB* gene DNA fragment to known *gyrB* gene DNA fragment sequences**. (Emphasis added.)

First, it is emphasized that the invention is directed to a method of identifying microorganisms. It is a series of steps that amplify and isolate the target DNA fragment to be compared with the known gyrB gene DNA fragment sequences. The method does not purport to identify any and all possible microorganisms by comparing the target sequence with any and all gyrB genes as found in any and all microorganisms. The invention is a process in which the target DNA sequence of a microorganism is compared to a known pool of gyrB genes for the purpose of identifying/classifying the microorganism based on sequence similarity or dissimilarity. There may arise a new DNA gyrase fragment that is so dissimilar to the known sequences that it may be identified/classified separately from the known sequences. A complete database of DNA gyrase for all microorganisms is not a prerequisite for the invention to operate; whether there is a complete database or not, the claimed invention can still synthesize, amplify, isolate, determine, and compare the determined DNA gyrase sequence to the known sequences to identify the microorganism. Additionally, a person of ordinary skill in the art of phylogenetic analysis would know that the phylogenetic relationship of a microorganism can be established based on degrees of similarity or dissimilarity of the determined gyrB sequence to the known gyrB sequences. There does not have to be necessarily an exact match to the known sequence to identify/classify the microorganism. (See, for example, Yamamoto, S. and Harayama, S. 1995. PCR Amplification and Direct Sequencing of *gyr B* Genes with Universal Primers and Their Application to the Detection and Taxonomic Analysis of *Pseudomonas putida* Strains. *Appl. Environ. Microbiol.* 61: 1104-1109; Yamamoto, S. and Harayama, S. 1996. Phylogenetic Analysis of *Acinetobacter* Strains Based on the Nucleotide Sequences of *gyr B* Genes and on the Amino acid Sequences of Their Products. *Int. J. Syst Bacteriol.* 46: 506-511; Yamamoto, S. and Harayama S. 1998. Phylogenetic relationships of *Pseudomonas putida* strains deduced from the nucleotide sequences of *gyr B*, *rpoD* and 16S rRNA genes. *Int. J. Syst Bacteriol.* 48: 813-819; Yamamoto S., Bouvet P. J. M. & Harayama, S. 1998. Phylogenetic structures of the genus *Acinetobacter* based on the *gyr B* sequences: Comparison with the grouping by DNA-DNA hybridization. *Int. J. Syst. Bacteriol.* (in press); Harayama, S. and Yamamoto, S. 1996. P hylogenetic Identification of Pseudomonas Strains Based on a Comparison of *gyr B* and *rpoD* Sequences. p. 250-258 in Molecular Biology of Pseudomonads, edited by T, Nakazawa, K. Furukawa, D Haas, S. Silver. ASM Press, Washington, D. C.: and Watanabe, K., Yamamoto, S.,

Hino, S. and Harayama, S. 1998. Population dynamics of phenol-degrading bacteria in activated sludge determined by *gyr B*-targeted quantitative PCR. *Appl. Environ. Microbiol.* 64: 1203-1209).

Furthermore, the assumption that genes for DNA gyrase or its isofunction enzymes should exists for all organisms does not require or support the proposition that there must be a complete and full database of DNA gyrase in order to practice the invention. Although the assumption forms an underlying motivation for the claimed invention, the claimed invention can still be practiced, *i.e.* it can still synthesize, amplify, isolate, determine, and compare, without any regard to the assumption. This assumption supports the proposition that the process can be applied most of the time, if not all of the time. If by remote chance that there is no DNA gyrase in the microorganism under examination, then the microorganism would simply not be identified/classified by this technique. Because there is no requirement that there be a complete and full database, there is no shifting of the burden of enablement to the public as indicated in the office action.

It is alleged in the office action that "the disclosure has not provided sufficient guidance as to which of the literally trillions of possible combinations are to be used and how these results are to be interpreted." Applicants submit that although there are a large number of combinations, it is perfectly clear which degenerate DNA sequences can be used from the amino acid sequence given in the claimed method. A person of ordinary skill in the art is directed to use a pair of DNA primers from the amino acid sequences given in the claim to hybridize the primers to the template DNA in order to amplify the gyrB gene in a microorganism. The specification gives adequate guidance to a person of ordinary skill in the art on how to do this. Merely the fact that there are a great number to choose the primers from does not render the claimed invention non-enabling. See, for example, Yamamoto et al., *Applied and Environmental Microbiology*, Mar. 1995, 61: 1104-1109, submitted with the IDS dated March 30, 2001, which describes the usage of universal degenerate primers for the amplification of DNA gyrase subunit B genes. Fig. 1 can also provide guidance on the choices of the primers based on the given amino acid sequences. Furthermore, results can be interpreted by a person of ordinary skill in the art using the known

art of phytogenetic analysis (see the references cited on page 11 of this response; those references are also provided on page 3 of the present specification).

It is further alleged in the Office Action that "the specification has not provided sufficient guidance as to how any other primer pair encodes any other amino acid sequence is to be used in interpreting the products." Claim 1 as well as other claims gives specific guidance as to which amino acid sequence can be used to produce the primer pairs. A person of ordinary skill in the art is enabled to carry out the claimed method and interpret the results using the known art of phytogenetic analysis.

Claims 1 to 16 have been amended to obviate the indefinite rejections. The term, "SEQ ID NO," was added wherever appropriate in the claims. The forward and reverse primers are known terms in the art. The forward primer is the codes read off from the amino acid sequence, with provision made for codon degeneracy. The reverse primer must be converted from the coding sequence chosen from the amino acid sequence to its complement (A->T, G->C, M->K, etc.) and then written in the reverse direction, nucleotide-by-nucleotide (not codon-by-codon). Thus, that the forward and reversed primers are based on the given amino acid sequences provided in the claims would be clear and understandable to a person of ordinary skill in the art.

For the foregoing reasons, Applicants believe that amended claims are now allowable and that the application is in condition for allowance.

Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be allowed. Enclosed is a check for the Petition for Extension of Time fee (two months). Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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